

US006995158B2

# (12) United States Patent

Rabelink et al.

(54) PHARMACEUTICAL PREPARATION
CONTAINING AT LEAST FOLIC ACID OR A
FOLATE AND TETRAHYDROBIOPTERIN
(BH4) OR DERIVATIVES THEREOF USED
FOR THE TREATING OR PREVENTING
CARDIOVASCULAR OR NEUROLOGICAL
DISORDERS BY MODULATION OF THE
ACTIVITY OF NITRIC OXIDE SYNTHASE
(NOS)

(75) Inventors: **Tom J. Rabelink**, Utrecht (NL); **Rudolf Moser**, Schaffhausen (CH)

(73) Assignee: Eprov A.G., Schaffhausen (CH)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35

U.S.C. 154(b) by 0 days.

(21) Appl. No.: 10/377,618

(22) Filed: Mar. 4, 2003

(65) **Prior Publication Data** 

US 2003/0216400 A1 Nov. 20, 2003

## Related U.S. Application Data

- (62) Division of application No. 09/588,301, filed on Jun. 7, 2000, now Pat. No. 6,544,994.
- (51) Int. Cl. A61K 31/50 (2006.01) A61K 31/195 (2006.01)

(10) Patent No.: US 6,995,158 B2

(45) **Date of Patent:** 

Feb. 7, 2006

(52) **U.S. Cl.** ...... 514/249; 514/565

See application file for complete search history.

### (56) References Cited

#### U.S. PATENT DOCUMENTS

4,752,573	A	6/1988	Ziegler et al.	
5,502,050	A	3/1996	Gross	
6,117,872	A	9/2000	Maxwell et al.	
6,544,994	B2*	4/2003	Rabelink et al 514/249	,

## OTHER PUBLICATIONS

M.C. Verhaar et al., "5-Methyltetrahydrogolate, the Active Form of Folic Acid, Restores Endothelial Function in Familial Hypercholesterolemia," *Circulation*, 97(3): 1998, pp. 237-241.

\* cited by examiner

Primary Examiner—Raymond J. Henley, III (74) Attorney, Agent, or Firm—Millen White Zelano & Branigan, P.C.

# (57) ABSTRACT

The invention relates to the uses of at least folic acid or a folate and tetrahydrobiopterin (BH<sub>4</sub>) or derivative thereof for treating or preventing cardiovascular of neurological disorders by modulation of the activity of nitric oxide synthase (NOS).

# 6 Claims, 7 Drawing Sheets